Art Unit: 1648

2

- 40. (Withdrawn and currently amended): An attenuated human rotavirus population, comprising a single variant or substantially a single variant, said variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7, wherein said VP4 single variant or substantially single variant is chosen from the group of: a VP4 variant, wherein the VP4 gene contains a thymine base (T) at position 501 from the start codon; and a VP4 variant, wherein the VP4 gene encodes a VP4 protein that contains a phenylalanine (Phe) at position 167 from the start codon; and wherein said VP7 single variant or substantially single variant is chosen from the group of: a VP7 variant, wherein the VP7 gene contains a thymine (T) at position 605 from the start codon; and a VP7 variant in which the VP7 gene codes for a VP7 protein that contains a methionine (Met) at position 202 from the start codon.
- 41. (Withdrawn): A rotavirus population according to claim 40 which is a cloned strain.
- 42. (Withdrawn): A rotavirus population according to claim 40 which is derived from a human rotavirus infection.
- 43. (Withdrawn): A rotavirus population according to claim 40 which replicates in and is excreted by humans.
- 44. (Withdrawn): A rotavirus population according to claim 40 in which the substantially single variant is a variant in which the VP4 gene comprises at least one substitution chosen from the group of: an adenine base (A) at position 788; an adenine base (A) at position 802; and a thymine base (T) at position 501 from the start codon.
- 45. (Withdrawn): A rotavirus population according to claim 44 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1.
- 46. (Withdrawn): A rotavirus population according to claim 40 in which the substantially single variant is a variant in which the VP7 gene comprises at least one substitution chosen from the group of: a thymine (T) at position 605; an adenine (A) at position 897; and a guanine (G) at position 897 from the start codon.
- 47. (Withdrawn): A rotavirus population according to claim 46 in which the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.
- 48. (Withdrawn): A rotavirus population according to claim 40 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.

Art Unit: 1648

(Withdrawn): A rotavirus which comprises a nucleotide sequence encoding a 49 VP4 protein wherein the nucleotide sequence is the nucleotide sequence set forth in SEQ ID NO:1, and a nucleotide sequence encoding a VP7 protein.

3

- (Withdrawn): A rotavirus population according to claim 40, designated as P43 50. and deposited under accession number ECACC 99081301.
- (Withdrawn): A rotavirus variant designated P43 and deposited with the 51. ECACC under accession number 99081301, rotavirus progeny and immunologically active derivatives thereof and materials obtained therefrom.
- (Withdrawn): A rotavirus reassortant comprising at least one antigen or at 52. least one segment of the rotavirus variant P43 of claim 50.
- (Withdrawn): A method of producing a purified human rotavirus population comprising a substantially single variant, the method comprising:

passaging a rotavirus preparation on a suitable cell line;

optionally selecting homogeneous culture using the steps of either:

limit dilution; or

individual plaque isolation; and

checking for the presence of a substantially single variant by sequencing an appropriate region of the VP4 and/or VP7 gene sequence.

- (Withdrawn): A method according to claim 53 in which the rotavirus 54. preparation is passaged on AGMK cells.
- (Withdrawn): A method according to claim 53 in which the rotavirus 55. preparation has the characteristics of an 89-12 strain or derivative thereof.
- 56. (Withdrawn): A method according to claim 53, which comprises the additional step of ether treatment to remove adventitious ether-sensitive contaminating agents.
- 57. (Previously presented): A vaccine composition comprising a live attenuated human rotavirus population virus, comprising a single variant or substantially a single variant, said variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 admixed with a suitable pharmaceutical carrier or adjuvant.
- 58. (Previously presented): A vaccine composition according to claim 57 adapted for oral administration.
- (Previously presented): A vaccine composition according to claim 58 in which the live attenuated virus is formulated with an antacid composition.

Art Unit: 1648

60. (Previously presented): A vaccine composition according to claim 59, wherein the antacid composition comprises an organic antacid.

- 61. (Previously presented): A vaccine composition according to claim 60, wherein the antacid is sodium citrate.
- 62. (Previously presented): A vaccine composition according to claim 59, wherein the antacid composition comprises an inorganic antacid.
- 63. (Previously presented): A vaccine composition according to claim 62, wherein the antacid is aluminium hydroxide.
- 64. (Previously presented): A vaccine composition according to claim 62, wherein the antacid is calcium carbonate.
- 65. (Previously presented): A vaccine composition according to claim 64, which further comprises a viscous agent.
- 66. (Previously presented): A vaccine composition according to claim 65, wherein the viscous agent is xanthane gum.
- 67. (Previously presented): A vaccine composition according to claim 64, wherein the live attenuated virus is formulated with calcium carbonate and xanthane gum and reconstituted with aqueous solution.
- 68. (Previously presented): A vaccine composition according to claim 59, wherein the live attenuated virus is formulated with the antacid composition and lyophilised in a blister pack.
- 69. (Previously presented): A vaccine composition according to claim 57, wherein the virus is in lyophilised form.
- 70. (Previously presented): A vaccine composition according to claim 69, wherein the live attenuated virus and the antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.
- 71. (Previously presented): A vaccine composition according to claim 69, wherein the live attenuated virus and the antacid composition are present in the same container for formulation as a lyophilised vaccine composition to be reconstituted with aqueous solution prior to administration.
 - 72. (Cancelled)

5

Art Unit: 1648

- 73. (Previously presented): A vaccine composition according to claim 69, wherein the composition is in the form of a quick dissolving tablet for immediate dissolution when placed on the tongue.
- 74. (Previously presented): A vaccine composition according to claim 69 comprising a lyophilised live attenuated rotavirus admixed with an inorganic antacid such as calcium carbonate and a viscous agent such as xanthane gum.
- 75. (Previously presented): A vaccine composition according to claim 74, wherein the attenuated virus and the antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.
- 76. (Previously presented): A vaccine composition according to claim 74, wherein the attenuated virus and the antacid composition are formulated in the same container, as a lyophilised vaccine composition to be reconstituted with aqueous solution prior to administration.
- 77. (Withdrawn): A method of manufacture of a rotavirus vaccine comprising admixing a lyophilised live attenuated human rotavirus with an antacid and a viscous agent.
- 78. (Withdrawn): A method of preventing rotavirus infection in humans by administering to a human subject in need thereof an effective amount of a vaccine according to claim 57.
- 79. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57, which is a cloned strain.
- 80. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57, which is derived from a human rotavirus infection.
- 81. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57, which replicates in, and is excreted by, humans.
- 82. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57 in which the substantially single variant is a variant in which the VP4 gene comprises at least one substitution chosen from the group of: an adenine base (A) at position 788; an adenine base (A) at position 802; and a thymine base (T) at position 501 from the start codon.
- 83. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 82 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1.

No.: 10/049,192

Art Unit: 1648

84. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57 in which the substantially single variant is a variant in which the VP7 gene comprises at least one substitution chosen from the group of: a thymine (T) at position 605, an adenine (A) at position 897 and a guanine (G) at position 897 from the start codon.

6

- 85. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 84 in which the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.
- 86. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and the VP7 gene comprises a nucleotide sequence set forth in SEO ID NO:2.
- 87. (Previously presented): A vaccine composition comprising a live attenuated rotavirus which comprises a nucleotide sequence encoding a VP4 protein wherein said VP4-encoding nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO:1, and a nucleotide sequence encoding a VP7 protein.
- 88. (Previously presented): A vaccine composition comprising a live attenuated rotavirus which comprises a nucleotide sequence encoding a VP4 protein and a nucleotide sequence encoding a VP7 protein wherein said VP7-encoding nucleotide sequence is set forth in SEQ ID NO:2.
- 89. (Previously presented): A vaccine composition comprising a live attenuated rotavirus population according to claim 57, designated as P43 and deposited under accession number ECACC 99081301.
- 90. (Previously presented): A vaccine composition comprising a live attenuated rotavirus variant designated P43 and deposited with the ECACC under accession number 99081301, rotavirus progeny and immunologically active derivatives thereof and materials obtained therefrom.
- 91. (Previously presented): A vaccine composition comprising a live attenuated rotavirus reassortant comprising at least one antigen or at least one segment of the rotavirus variant P43 of claim 89.

Please add the following new claims:

92. (New): A vaccine composition comprising a live attenuated rotavirus population according to claim 57 in which the substantially single variant is a variant in which the VP4 gene encodes a VP4 protein, wherein a phenylalanine (Phe) is present at position 167 from the start codon.

Art Unit: 1648

7

93. (New): A vaccine composition comprising a live attenuated rotavirus population according to claim 57 in which the substantially single variant is a variant, wherein the VP7 gene encodes a VP7 protein in which a methionine (Met) is present at position 202 from the start codon.